Program/Abstract # 149
Xenopus ADAM19 is critical for neural and muscle development
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ADAM19 is a member of the meltrin subfamily of ADAM metalloproteases. ADAM19 is transmitted as a maternal transcript with zygotic expression beginning in the dorsal blastopore lip at gastrula stage. ADAM19 mRNA expression increases through neurulation and tailbud formation, becoming enriched in dorsal neural and mesodermal derived structures. Using Morpholino knock down, we show that a reduction of ADAM19 protein in gastrula stage embryos results in a decrease of Brachyury expression in the notochord concomitant with an increase in the dorsal markers, Goosecoid and Chordin. These changes in gene expression occur while the blastopore closes at the same rate as the control embryos. During neurulation and tailbud formation, ADAM19 knock down reduces the expression of the neural markers N-tubulin and NRP1 but not Sox2. In the somitic mesoderm, the expression of MLC is also decreased while MyoD is not. ADAM19 knock down also reduces ADAM11 and Twist, two markers of the cranial neural crest cells. Using targeted microinjection, we show that the reduction of neural and neural crest markers is a direct result of ADAM19 knock down in these tissues and not a secondary effect of perturbing the dorsal mesoderm patterning. Thus ADAM19 appears to control the specification of muscle, neurons and cranial neural crest cells.

doi:10.1016/j.ydbio.2008.05.161

Program/Abstract # 150
Maintaining the balance: Regulation of Cadherin-11 by ADAM13 during cranial neural crest migration in _Xenopus laevis_
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The *C*ranial *N*eural *C*rest (CNC) is a transient population of cells that undergo a large-scale migration imperative to craniofacial development. Cell adhesion molecules such as members of the Cadherin superfamily are essential for this process. Cadherin-11, a "mesenchymal" cadherin, is expressed throughout CNC migration in *Xenopus laevis*. While too much of this cell adhesion molecule predictably blocks migration, too little of this molecule has a similar effect. This observation suggests that Cadherin-11 protein levels are tightly regulated on the surface of the migrating cells. Our findings show that Cadherin-11 is cleaved during *Xenopus* CNC migration, and that ADAMs (*A D*isintegrin *A*nd *M*etalloprotease) from the meltrin subfamily are responsible for this event. ADAM13 is the most likely ADAM to cleave Cadherin-11 during CNC migration because its expression is restricted to the CNC and it associates with Cadherin-11 *in vivo*. Our results suggest that ADAM13 regulation of Cadherin-11 plays a crucial role in CNC migration since blocking ADAM13 activity inhibits both Cadherin-11 cleavage and CNC migration. Additionally, ADAM13 overexpression rescues CNC migration in embryos also overexpressing Cadherin-11.We have also found that the extracellular cleavage fragment of Cadherin-11 retains biological activity and promotes CNC migration, most likely by binding to full-length Cadherin-11 molecules to decrease cell adhesion. And lastly, unlike ADAM10 cleavage of N-Cadherin and E-Cadherin, ADAM13 cleavage of Cadherin-11 does not affect its interaction with beta-catenin, nor promote downstream signaling through this molecule.

doi:10.1016/j.ydbio.2008.05.162

Program/Abstract # 151
ADAM metalloprotease control of cell specification and cell migration during early embryogenesis
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The control of cell adhesion and motility are two key elements that regulate morphogenetic movements. ADAMs (protein containing *A D*isintegrin *A*nd *M*etalloprotease) are cell surface metalloproteases that have been linked to both cell signaling and cell motility. While studies of ADAM signaling have identified many substrates including EGF ligands, Notch and Ephrins, the control of cell motility is less well understood. We have cloned ADAM9, 13 and 19 to study their function during early embryogenesis. Using combinations of grafts, live cell imaging, and molecular approaches, we show that ADAM13 is involved in cranial neural crest cell migration by cleaving Cadherin-11. The cleavage of Cadherin-11 releases the homophilic binding site that in turn can stimulate cell migration. The remaining transmembrane region can still bind to β-catenin, prevent its translocation to the nuclei to induce gene expression, and in effect regulate the Wnt/β-catenin signaling. In the absence of ADAM13, ADAM9 protein level increases and together with ADAM19 these proteases can compensate for the loss of ADAM13 to promote CNC migration. While ADAM13 and 19 are very similar in structure, ADAM19 function appears to be mostly in cell specification. ADAM19 is essential for dorsal mesoderm patterning during gastrulation and later during tailbud formation. In addition, ADAM19 expression in the ectoderm is critical for proper neuronal and neural crest cell induction. This function is not shared and is not compensated by ADAM13. Thus, the *Xenopus* system allows us to precisely dissect and visualize ADAM protein function during morphogenesis.

doi:10.1016/j.ydbio.2008.05.163

Program/Abstract # 152
Characterization of a new factor in the non-canonical Wnt signaling
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The Wnt signaling pathway has crucial roles in a variety of developmental processes. The non-canonical Wnt pathway involves regulation of the cell polarity and motility. But the signaling process from stimulation in plasma membrane to regulation in actin cytoskeleton remains to be explored. Our lab has previously identified the Formin homology protein, Daam1, which mediates Wnt-induced cytoskeletal changes but how Daam1 accomplishes this remains unknown. In a screen for effectors of Daam1, we have identified the protein "Missing In Metastasis" or MIM as a major interactor of Daam1. Through co-immunoprecipitation experiment, we found that the association of Daam1 and MIM is positively regulated by Wnt signaling. The co-localization of endogenous Damm1 and MIM was revealed by immunofluorescence experiment. We have also shown that overexpression of MIM will cause the disassembly of stress fibers and induce actin-rich protrusions. The depletion of endogenous MIM in *Xenopus* by a Morpholino specifically induces anterior neural tube closure defects. Our results taken together suggest that MIM is a factor downstream of Daam1 in the non-canonical Wnt pathway that